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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,404	08/18/2003	Takayuki Tanaka	59753 (48185)	3999

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,404	TANAKA ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed 01/18/06, claim 3 has been amended. Claims 1-4 are currently pending for prosecution on the merits.

Response to Arguments

2. Applicant's arguments with respect to claims 1-4 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the restenosis or neointimal formation caused by percutaneous transluminal coronary angioplasty (PTCA) or a coronary-artery bypass graft (CABG) with 3-methyl-1-phenyl-2-pyrazolin-5-one, does not reasonably provide enablement for the term "prevention and/or therapy wall injury" with administration of a compound of the formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of

the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The inventions relate to a method of preventing or treating arterial wall injury with the administration of said compounds represented by the formula (I). The instant specification broadly defines the term "arterial wall injury" as "neointimal formation, the testernosis or reocclusion of vascular lumens or decrease in elasticity and flexibility".

There are no known compounds of similar structure which have been demonstrated to prevent or cure the claimed conditions encompassed by the instant claims. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "magic bullet" is contrary to our present understanding of pharmacology. For instance, there is no known cure for hypertension (see The Merck Manual, Section 16, Chapter 199, 2006).

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. It is beyond the skill of pharmacologists today to get a single agent to treat all types of "arterial wall injury" encompassed by the instant claims.

The scope of the instantly claimed "arterial wall injury" is very broad. It includes not only injury caused by PTCA or CABG, for example reointimal formation or restenosis caused by PTCA or CABG, but also various other diseases characterized by "decrease in elasticity and flexibility" or "reocclusion of vascular lumens", for exmple hypertension, atherosclerosis or

Fabry disease. In addition, the breadth of the claims is further exacerbated by the instantly claimed plethora of compounds represented by the formula (I).

The specification discloses study showing the efficacy of 3-methyl-1-phenyl-2-pyrazolin-5-one (edaravone) in decreasing neointimal formation caused by balloon injury to the abdominal aorta or carotid artery of the animal (i.e., rabbits or rat)(Examples). However, there is no demonstrated correlation the tests and results apply to all of "arterial wall diseases" embraced by the instant claims.

As discussed above, the skill artisan would have not known from the instant tests that the claimed compounds would be able to treat all of "arterial wall injuries". Furthermore, the skill artisan would have not known that which compounds of the formula are capable of accomplishing the desired result of the claimed invention without undue amount of experimentation. The specification does not provide sufficient guidance in how to use vast number of possible compounds represented by the formula, other than 3-methyl-1-phenyl-2-pyrazolin-5-one (edaravone). The specification provides no guidance, in the way of enablement for the full scope of all compounds that are potentially suitable for the invention work similarly as to 3-methyl-1-phenyl-2-pyrazolin-5-one (edaravone).

Therefore, the skill artisan would turn to undue amount of trial and error to find out which airway disease would be responsive to the claimed composition.

In view of limited numbers of working examples, the insufficient amount of guidance present in the specification, the nature of the invention, the state of art, the breadth of the claim and the relative skills of the artisan and the predictability of the pharmaceutical art where many specific differences or different physicochemical properties are existed among unrelated

structural compounds would take "undue painstaking experimentation" to practice the invention commensurate in scope with these claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishi et al. (US 4857542).

Nishi teaches the administration of compound(s) represented by the formula I (i.e., 3-mehtyl-1-phenyl-2-pyrazolin-5-one) to mammals including human to treat or prevent circulatory disorders, wherein said compound(s) is administered at a dose of 1 to 100mg 1 to 3 times/day (oral), at a dose of 0.01 to 10 mg 2 to 5 times/day (intravenous injection, or at a dose of 1 to 100mg 1 to 3 times/day (intrarectal administration).

Although Nishi is silent about the prophylactic utility of said compound in preventing arterial wall injury, namely percutaneous transluminal coronary angioplasty (PTCA), coronary-artery bypass graft (CABG) or restenosis or neointimal formation after percutaneous transluminal coronary angioplasty or coronary-artery bypass graft, such prophylactic utility deems to be inherent the referenced method. The prior art directing administration of the same compound(s) inherently possessing therapeutic effect, in overlapping dosage amounts, as disclosed by Applicant anticipates the Applicant's invention even absence of underlying mechanism. Applicant's attention is directed to Ex parte Novitski 126 USPQ 1389 (BOPA 1993)

illustrating anticipation resulting from inherent use, absent a haec verba recitation for such prophylactic utility. In the instant case, as in Ex parte Novitski, the claims are directed to preventing a malady or disease with old and well known compounds of compositions. The prior art administering compounds inherently possessing a protective utility anticipates claims directed to such protective use.

Conclusion

5. No Claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614